Frequent Disease Relapse after Withdrawal of Dendritic Cells Imprint Pro-inflammatory Gut 2021; –

CD 23.7% (9/38) 51.4% (19/37) 63.3% (19/30) 75% (15/20)
UC 20% (5/25) 31.6% (6/19) 52.6% (10/19) 78.6% (11/14)
IBD total 22.2% (14/63) 44.6% (25/56) 59.2% (29/49) 76.5% (26/34)

Abstract P104 Table 1

P104 FREQUENT DISEASE RELAPSE AFTER WITHDRAWAL OF INFILIXIMAB IN IBD PATIENT WITH SUSTAINED REMISSION

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Introduction In the UK, NICE guidance recommends annual review of biologics, with withdrawal of therapy in all patients in remission. This study retrospectively evaluates disease course following withdrawal of infliximab in IBD patients with sustained remission.

Primary Outcome Relapse free survival.

Secondary Outcomes Identification of predictors of relapse and evaluation of response to future therapy.

Methods IBD patients from Royal London Hospital who ceased infliximab due to sustained remission were identified. The following information was obtained from electronic patient records: demographics, Montreal classification, immunomodulator use, clinician determined relapse, objective evaluation of disease activity within 3 months prior to treatment cessation and 6/12/18/24 months following cessation (CRP>5, calprotectin>50, endoscopic, radiological), steroid use at relapse, subsequent biologic use and outcome Analysis was undertaken for total IBD, CD and UC. Survival analysis and logistical regression was calculated using SPSS®.

Results 75 patients were identified. CD:UC = 43:32; F:M = 34:41; median age = 31.3 years (IQR 41.15–40.75), median duration of follow up = 21.1 months (IQR 11.1–44.2), Asian:Black:Caucasian:Unknown = 16:3:4:79. The median relapse free survival for CD was 12.4 months (IQR 10.4–14.4) and for UC was 18.2 months (IQR 10.5–25.9). Relapse rates for patients who had completed follow up for each time point are presented in table:

In univariate analysis, perianal disease and L3 disease were negatively associated with relapse at 1 year for patients with CD (perianal OR 0.87 CI 0.09–0.81 p=0.03 and L3 OR 0.18 (comparator L1) CI 0.04–0.87 p=0.03). However significance was lost when multivariate analysis was undertaken. Following relapse, 43.1% (19/44) required steroids and 88.6% (39/44) restarted a biologic, 69.2% (30/44) restarting infliximab. Of those who restarted infliximab, 56.7% (17/30) responded to standard therapy, with 10% (3/30) requiring dose escalation. 33.3% (10/30) required alternative therapy.

Conclusion Within 24 months of cessation 76.5% patients relapsed. The majority of these restarted a biologic. However, only 56.7% patients who restarted infliximab responded to standard dose. With additional costs of newer biologics and morbidity of disease flare and steroid use, routine withdrawal of TNF antagonists should only occur after careful consideration.

P105 DENDRITIC CELLS IMPRINT PRO-INFLAMMATORY α4β7 +CLA+ T CELLS WITH POTENTIAL FOR GUT AND SKIN HOMING

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Background Integrin α4β7 induced on T cells during activation in intestinal lymphoid enables selective homing to the intestinal mucosa. Retinoic acid (RA) produced by the activating dendritic cell (DC) induces α4β7 and also inhibits the fucosyltransferase FUC-T VII that otherwise generates the selectin ligand CLA required for skin homing. Therefore, antigen experienced T cells are generally either gut tropic (α4β7+) or skin tropic (α4β7-CLA-). We hypothesised the existence of additional ‘dual tropic’ (α4β7+CLA+) T cells, generated in the gut but with capacity to traffic to skin; such cells could explain skin inflammation in inflammatory bowel disease (IBD). Here, we report the generation of dual tropic cells in vitro and characterise the population in blood.

Methods Using flow cytometry, expression of α4β7 and CLA was assessed on ex vivo T-cells in whole blood and on proliferating cells generated by stimulation of naïve CD4+ T cells with monoclonal antibodies (anti-CD3/28/2), or with allogeneic colonic or monocyte-derived DC (moDC). Cultures were in the presence or absence of serum, monoclonal antibodies, RA receptor (RAR) antagonist, or conditioned media. Expression of FUCT-VII was assessed by qRT-PCR.

Results T-cells activated with antibodies expressed β7 but not CLA. Inhibition of RARα signalling and removal of serum reduced β7 expression and induced both CLA and FUCT-VII expression, suggesting endogenous RARα signalling shapes homing phenotype in these cultures. In contrast, activation with DC (colonic or RA-generating moDC), generated CLA+ T cells, including a population which co-expressed β7. Conditioned medium from DC stimulated cultures did not induce CLA on antibody-activated cells.

Activation by DC or in the presence of the RARα antagonist both led to increased expression of FUCT-VII. However,